Oral Presentation - 17

Co-Infusion of Fructose-1, 6-Diphosphate Improves Survival in Propranolol Poisoning Compared with Adrenaline Infusion Alone in A Rodent Model of Poisoning

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Abstract

Objectives: FDP is an intermediary metabolite in the glycolytic pathway. Exogenous administration increases metabolic yield of ATP from anaerobic glycolysis, reduces lactate production, and mitigates development of tissue ischemia in shock states. FDP infusion has beneficial effects on survival and haemodynamics in shock and ischaemic tissue. Propranolol is a beta-receptor antagonist which produces severe hypotension in overdose. We have previously reported a beneficial effect of FDP infusion on survival and haemodynamics in severe propranolol poisoning.

Hypothesis: Exogenously administered FDP will improve the response to other inotropic agents used in the treatment of propranolol poisoning.

Method: Adult, male Wistar rats (n=10 per group) were anaesthetised, ventilated and instrumented to record heart rate, blood pressure and cardiac output. Propranolol (24mg/kg/h) was infused until blood pressure fell to 50% of baseline, and then halved to maintain toxicity. Animals received one of five treatments: 10%FDP, escalating adrenaline dosing, 10%FDP+ escalating adrenaline dosing. We also assessed high-dose insulin and high-dose insulin+10%FDP. 10% Glucose was used as control infusion arm. Animals were monitored for 180 minutes. Fluid volumes were matched for groups. Outcomes included number of animals surviving and response of haemodynamic parameters to treatment. Survival assessed by Log-rank (Mantel-Cox) test. Hemodynamic significance assessed by 1-way ANOVA at individual time points.

Results: FDP+Adrenaline was associated with increased length of survival (Median=172 min v 75 min IV Glucose [p=0.03, Hazard Ratio 4.1] and 172 v 105 min adrenaline [p=0.01, HR 4.4]) and higher MAP at a number of time points compared to control, adrenaline and FDP alone. Adrenaline dose did not differ when FDP was administered. Insulin+FDP also resulted in a significant survival benefit over glucose or adrenaline alone (Median=180 min v 75 min Gluc [p=0.036, HR 4.1] and 105 min Adrenaline [p=0.03, HR 4.0]). FDP alone did not improve survival significantly.

Conclusions: Co-administration of FDP with adrenaline or insulin may confer benefits to either agent alone in propranolol poisoning; some of this effect may be the result of FDP being a substrate for anaerobic glycolysis. However, the cellular protective effects of FDP in ischaemic tissue may also play a role. Assessment of the effects of FDP on catecholamine sparing, in particular, in the clinical setting of cardiovascular drug poisoning are warranted.